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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/692,071 | 10/22/2003 | Brian K. Kobilka | STAN-213CIP | 8423 |
| 24353 | 7590 | 03/18/2005 | EXAMINER | |
| BOZICEVIC, FIELD & FRANCIS LLP 1900 UNIVERSITY AVENUE SUITE 200 EAST PALO ALTO, CA 94303 | | | LI, RUIXIANG | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1646 | |

DATE MAILED: 03/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/692,071 | Applicant(s) KOBILKA ET AL. | |
| | Examiner Ruixiang Li | Art Unit 1646 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13 and 16-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13 and 16-21 is/are rejected.
- 7) ☒ Claim(s) 22 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' amendment filed on December 20, 2004 has been entered in full. Claims 1-12, 14, and 15 have been canceled. Claim 13 has been amended. Claims 16-22 have been added. Claims 13 and 16-22 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Withdrawn Objections and/or Rejections

The rejection of claim 13 under 35 U.S.C. 102(b) as being anticipated by Gether et al. as set forth at page 3 of the previous Office Action (Paper No. 09272004, mailed on 09/29/2004), has been withdrawn in view of Applicants' amendment to the claim.

The objection to claim 13 for depending upon non-elected claims has been withdrawn in view of Applicants' amendment to the claim.

Claims Rejections under 35 U.S.C. 102(b)

(i). Claims 13, 16, and 18 are rejected under 35 U.S.C. 102 (b) as being anticipated by Cochet et al. (J. Biol. Chem. 263:3290-3295, 1988).

Cochet et al. teach that EGF receptor is a single chain polypeptide composed of three major domains: a large extracellular ligand binding domain, a single hydrophobic membrane spanning domain, and a cytoplasmic domain (ref. Claim 13, MSST). The binding of EGF to the EGF receptor causes conformational change and dimerization of the EGF receptor, which is important for the transmembrane signaling of the EGF receptor (page 3290). Specifically, Cochet et al. teach epidermal growth factor-induced dimerization of EGF receptor in membrane preparation and in living cells using a water soluble chemical covalent cross-linking agent, EDAC (ref. claim 16, a chemical label) (see, e.g., abstract; page 3291). The dimer of the EGF receptor formed upon activation by EGF is determined by SDS-gel electrophoresis and immunoblotting on a nitrocellulose filter (ref. claim 13, a immobilization phase to which the receptor protein is attached) (page 3291). Since the cross-linking agent EDAC is water soluble and the dimerization was determined using EGF receptor in the membrane preparation and in living cells, the cross-linking agent was expected to attach in the extracellular domain, which is sensitive to the binding of EGF to its receptor. Thus, the reference of Cochet et al. meets the limitations of claims 13, 16, and 18.

(ii). Claims 13, 16, and 18-20 are rejected under 35 U.S.C. 102 (b) as being anticipated by Farahbakhsh et al. (Science 262:1416-1419, 1993).

Farahbakhsh et al. teach photoactivated conformational changes in a G protein coupled receptor, rhodopsin. Specifically, Farahbakhsh et al. teach conformational changes of rhodopsin detected by the EPR spectra of spin-labeled

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rhodopsin. The spin label (a chemical label) is attached to Cys¹⁴⁰ in a sensitive region (2nd intracellular loop) of the molecule where changes occur during photoactivation (See, Fig. 1, Fig. 2, A; 2nd paragraph of middle column of page 1418). Since Farahbakhsh et al. teach measuring the EPR spectra of spin-labeled rhodopsin, Farahbakhsh et al. inherently teach a cuvette (a immobilization phase) where the sample of the labeled rhodopsin was held and expected to attach. It is known in the art that the rhodopsin antagonist, 11-cis-retinal, is covalently bound in the middle of helices, inactivating the protein in the dark state. Light causes the isomerization of 11-cis retinal to the all-trans form and activates the receptor as evidenced by Dunham et al. (J. Biol. Chem. 274:1683-1690, 1999). Thus, the reference of Farahbakhsh et al. meets the limitations of claims 13, 16, and 18-20.

(iii). Claims 13 and 16-21 are rejected under 35 U.S.C. 102 (b) as being anticipated by Dunham et al. (J. Biol. Chem. 274:1683-1690, 1999).

Dunham et al. teach conformational changes in rhodopsin upon photoactivation using a series of rhodopsin mutants containing single reactive cysteine residues in the cytoplasmic side of helix F (3rd intracellular loop)(see Fig. 1; abstract; the middle of right column of page 1685), including the mutant V250C. The cysteine mutants were studied in two ways, by measuring their reactivity to a cysteine-specific reagent (PyMPO-maleimide) and by labeling the cysteins with a fluorescence label (monobromobimane) followed by fluorescence spectroscopic analysis (Abstract). Since the fluorescence change was measured in a 4-mm black acketed cuvette (4th paragraph of left column of page 1685), the rhodopsin receptor

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would be attached to cuvette (a immobilization phase). Dunham et al. also teach that the rhodopsin antagonist, 11-cis-retinal, is covalently bound in the middle of helices, inactivating the protein in the dark state. Light causes the isomerization of 11-cis retinal to the all-trans form and activates the receptor (page 1683). Thus, the reference of Dunham et al. meets the limitations of claims 13 and 16-21.

Claim Objection

Claim 22 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the


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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.


Ruixiang Li, Ph.D.
Examiner
March 9, 2005